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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/786,648	03/07/01	WILLIAMS	N	7438

026850 HM12/0814
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EXAMINER	
FORD, V	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/786,648	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS C

- Extensions of time may be available under t be timely filed after SIX (6) MONTHS from the mailing date
- If the period for reply specified above is less) days will be considered timely.
- If NO period for reply is specified above, the from the mailing date of this communication.
- Failure to reply within the set or extended pe ONED (35 U.S.C. § 133).
- Any reply received by the Office later than th filed, may reduce any earned patent term adjustment. See 37 CFF

file

Status

1)☒ Responsive to communica

2a)☐ This action is **FINAL**.

3)☐ Since this application is in prosecution as to the merits is closed in accordance with , 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-7 and 12-28* is

4a) Of the above claim(s) *1,6* deration.

5)☐ Claim(s) _____ is/are allowe

6)☒ Claim(s) *13-18 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's response to the Restriction requirement filed in Paper No. 6 filed on July 25, 2001 is acknowledged. Applicant's election of Group II with traverse, claims 13-18 and 27 is acknowledged. Claims 1, 6-7, 12, 19-26 and 28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being to a non-elected invention.

The traversal is on the grounds that Groups I-V are believed to be so linked as to form a single general inventive concept. These arguments have been fully considered but are not found to be persuasive for the reasons below:

Claim 1 of Group I is the main invention in this application and lacks novelty, therefore the other claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept.

Restriction is required under 35 U.S.C. 121 and 372.

The MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each (see MPEP 802.01). In the instant situation, Group I is drawn to a substance and pharmaceutical composition comprising one or more amino acid sequences. Group II is drawn to a

polypeptide. Group III is drawn to a composition comprising the peptide of claim 13 and an antigen. Group IV is drawn to a composition comprising the peptide of claim 13 and an antibody. Group V is drawn to a method of treating a subject having diarrhea.

Lack of unity exists when a technical relationship among the claimed inventions involving one or more of the same or corresponding "special technical features". A special technical feature is defined as a contribution which each of the inventions, considered as a whole, makes over the prior art. Group I lacks novelty under PCT Article 33(2) as being anticipated by Mirelman et al, *WO 95/29701, published November 9, 1995)*. Mirelman et al discloses conjugates of antigenic material selected from the group of a toxin, or fragment thereof, a toxoid and/or an adherence antigen derived from an infecting agent wherein the said antigenic material is covalently bound to a physiologically acceptable inert carrier, such as silica, chemically-modified silica, aluminum silicate, kaolin or latex. Therefore, Group I is the main invention in this application and it lacks novelty, therefore the other claims are not so linked by a special technical feature within the meaning of PCT Rule 13.2 so as to form a single inventive concept.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Specification Objections

2. The specification is objected because of what appear to be typographical errors. For example, page 6, line 6 the term "susbstance" should be changed to "substance" and page 17, line 18 the term "maximise" should be changed to "maximize". The applicant is asked to review the entire specification for spelling errors and correction is required.

Drawings

3. The drawings are objected to by the Draftsman under 37 CFR 1.84 or 1.152. See the attached form PTO 948.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 13-18 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses SEQ ID NO: 2, 3, 4 and 5 which corresponds to the amino acid sequence that encodes the claimed peptide. Claims 13-18 and 27 are directed to sequences that are between 75-85% homologous to SEQ ID NO: 2, 3, 4, 5 and corresponding sequences that are mixtures, homologues, variants and derivatives

that have a variant degree of identity (similarity, homology), and so forth. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 2, 3,4 and 5 the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO: 2, 3, 4 and 5 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded

that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 13-18 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 13-18 recite "exhibit activity the same or similar to EtxB or CtxB", it is unclear as to what the applicant is referring?

6. Claims 13-18 and 27 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because the abbreviations EtxB and CtxB are used. The proper name of the toxins should be "*Escherichia coli* heat labile entertoxin B" and "cholera toxin B", respectively used at the first occurrence of these terms in the claims or specification.

7. Claim 27 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 27 recites "EtxB/CtxB" it is unclear as to what the applicant is referring? Does this term mean *Escherichia coli* heat labile entertoxin B and cholera toxin B?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 13-18 and 27 are rejected under 35 U.S.C. 102(b) as anticipated by Loosmore et al, *(WO 96/26282, published August 29, 1996).*

Claims 13-18 and 27 are drawn to a peptide selected from the group consisting of SEQ ID NO 2, 3, 4 and 5, mixtures thereof, homologues, variants, and derivatives, which exhibit activity the same or similar to EtxB or CtxB but wherein the peptide does not exhibit GM-1 binding activity and has 75% homology to SEQ ID NOs. 2,3,4 and 5.

Loosmore et al disclose non-*Bordetella* gene products which may be one of a wide variety of proteins and polypeptides. The protein or peptide may be an enzyme, enzyme inhibitor, an antigen, an immunogen, an allergen, a hormone, a lymphokine, an immunoglobulin, a toxin, a toxin subunit, mammalian protein, a structural protein or receptor (p. 4-5). Loosmore disclose a cholera toxin molecule as the non-*Bordetella* gene product, specifically the B subunit of cholera toxin (p. 5). Loosmore et al teach a peptide sequence which is 100 % similar to SEQ ID NOs. 2,3,4 and 94% similar to SEQ ID No. 5 of the instant application. Therefore, it would be inherent that the peptide sequence of the prior art would exhibit activity the same or similar to EtxB or CtxB but not exhibit GM-1 binding activity. It would also be inherent that the peptide of the prior

art is an isolated fragment of the β4-α2 loop of the EtxB/CtxB and exhibits 85% homology to SEQ ID NO 2. Loosmore et al disclose the amino acid sequence in Figure 1 (page 35).

Since the Office does not have the facilities for examining and comparing applicant's peptide with the peptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the peptide of the prior art does not possess the same material structural and functional characteristics of the claimed peptide). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 13-18 and 27 are rejected under 35 U.S.C. 102(b) as anticipated by Arntzen et al, *WO 96/12801, published May 2, 1996).*

Claims 13-18 and 27 are drawn to a peptide selected from the group consisting of SEQ ID NO 2, 3, 4 and 5, mixtures thereof, homologues, variants, and derivatives, which exhibit activity the same or similar to EtxB or CtxB but wherein the peptide does not exhibit GM-1 binding activity and has 75% homology to SEQ ID NOs. 2,3,4 and 5.

Arntzen et al teach oral vaccines and oral adjuvants which are produced in transgenic plants and then administered through the consumption of the transgenic plant. DNA sequences both natural and synthetic encoding for the expression of immunogenic agents which are capable of causing an immune response in animals when fed in edible plants, plant tissues or derived plant materials are constructed and plants transformed for stable or transient expression in plant cells. Arntzen et al

disclose that their invention provides the first known functional method for immunizing animals via transgenic plants, where the plants express bacterial antigens that act as both immunogens and adjuvants when transgenic plant material expressing the antigen is fed to animals (see Abstract). Arntzen et al teach a peptide sequence which is 100 % similar to SEQ ID NOs. 2,3,4 and 94 % similar to SEQ ID NO. 5 of the instant application. Therefore, it would be inherent that the peptide sequence of the prior art would exhibit activity the same or similar to EtxB or CtxB but not exhibit GM-1 binding activity. It would also be inherent that the peptide of the prior art is an isolated fragment of the β4-α2 loop of the EtxB/CtxB and exhibits 85% homology to SEQ ID NO 2. Arntzen et al disclose the amino acid sequence on pages 100-101.

Since the Office does not have the facilities for examining and comparing applicant's peptide with the peptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the peptide of the prior art does not possess the same material structural and functional characteristics of the claimed peptide). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Pertinent Prior Art

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure, *(Mirelman et al, WO 95/29701, published November 9, 1995 and* Holmgren et al, *(WO 96/34893, published November 7, 1996).*

Status of Claims

11. No claims are allowed.

Conclusion

12. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
August 2, 2001

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